

IN THE SPECIFICATION

Please insert the following new paragraph on page 1 immediately following the paragraph added by amendment on July 22, 2003 (*i.e.*, the claim to priority benefit).

This application contains subject matter that is related to U.S. patent application Serial No. 10/627,990, filed on July 28, 2003.

Please amend the paragraphs at page 1 line 14 – page 2 line 11 as follows.

To date, various transdermal delivery systems (TDS) for the administration of rotigotine have been described. ~~WO 94/07568~~ WO 94/07468 discloses a TDS containing rotigotine hydrochloride as active substance in a two-phase matrix, which is essentially formed by a hydrophobic polymer material as the continuous phase and a disperse hydrophilic phase contained therein and mainly containing the drug and hydrated silica. The silica is said to enhance the maximum possible loading of the TDS with the hydrophilic salt. Moreover, the formulation of ~~WO94/07568~~ WO 94/07468 usually contains additional hydrophobic solvents, permeation promoting substances, dispersing agents and, in particular, an emulsifier which is required to emulsify the aqueous solution of the active component in the lipophilic polymer phase. A TDS prepared by using such a system has been tested in healthy subjects and Parkinson's patients. However, no satisfactory drug plasma levels were achieved.

Various further ~~TDS~~ TDSs have been described in WO 99/49852. ~~The TDS used in this patent application comprises a backing layer, inert with respect to the constituents of the matrix, a self-adhesive matrix layer containing an effective quantity of rotigotine hydrochloride or rotigotine, which contains a substantial amount of rotigotine hydrochloride (>5% w/w), and a protective film, which is to be removed before use. The matrix system is composed of a non-aqueous polymer adhesive system, based on acrylate or silicione, with a solubility of rotigotine of at least 5% w/w. Said matrix has been described as being essentially free of inorganic silicate particles.~~

~~However, even the TDS described in WO 99/49852 leave something to be desired as regards the obtainable flux rates of drug across human skin.~~

In the TDS according to ~~WO 94/07568~~ WO 94/07468 and many related applications, passive diffusion membranes were used.

Please amend the paragraph at page 3 lines 6-27 as follows.

~~These objects are solved by providing~~ There is now provided a TDS comprising a backing layer inert to the components of the matrix, a self-adhesive matrix containing rotigotine, and a protective foil or sheet to be removed prior to use,

characterized in that

the self-adhesive matrix ~~consists of~~ comprises a solid or semi-solid semi-adhesive polymer

- (1) wherein rotigotine in its free base form ~~has been~~ is incorporated,
- (2) which ~~is saturated with rotigotine and contains said rotigotine as~~ comprises a multitude of microreservoirs within the matrix, said microreservoirs containing rotigotine and optionally at least a crystallization inhibitor,
- (3) which is highly permeable [[for]] to the free base of rotigotine,
- (4) which is substantially impermeable [[for]] to the protonated form of rotigotine,
- (5) wherein the maximum diameter of the microreservoirs is less than the thickness of the matrix.

Please amend the paragraph at page 9 line 33 – page 10 line 2 as follows.

The self-adhesive matrix of the TDS of the present invention ~~consists of~~ comprises a solid or semi-solid semi-permeable polymer. Usually this polymer will be a pressure sensitive adhesive (PSA) or a mixture of such adhesives. The pressure sensitive adhesive(s) form a matrix in which the active ingredient and the other components of the TDS are incorporated.